UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,934	06/24/2003	Baskaran Chandrasekar	201267.90011	1854

26710 7590 08/27/2007

QUARLES & BRADY LLP
411 E. WISCONSIN AVENUE
SUITE 2040
MILWAUKEE, WI 53202-4497

EXAMINER	
CARTER, KENDRA D	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
08/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/602,934	CHANDRASEKAR ET AL.	
	Examiner	Art Unit	
	Kendra D. Carter	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,16,17,20-24,26,27,30-33 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,10,16,17,20-24,26,27,30-33 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of May 24, 2007 made to the office action filed November 24, 2006. Claims 9-10, 16-17, 20-24, 26-27 and 30-33 and 39 are pending in the application. Claims 1-8, 11-15, 18-19, 25, 28-29, and 34-38 are cancelled and claim 39 is new.

The restriction requirement is now moot because of the cancellation of claims 34-38.

For the reasons in the previous office action and below, the Applicant's arguments of the 35 U.S.C. 103(a) rejection of claims 9-10, 16-17, 20-24, 26-27, 30 and 32-33 as being unpatentable over Ungs (US 5,866,561) were found not persuasive, and thus upheld.

For the reasons in the previous office action and below, the Applicant's arguments of the 35 U.S.C. 103(a) rejection of claim 31 as being unpatentable over Ungs (US 5,866,561) further in view of Barry (US 5,439,446) were found not persuasive, and thus upheld.

Due to the amendment to the claims and the new claim, the modified 35 U.S.C. 103(a) rejections are made below.

The applicant's arguments are addressed below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 39 recites the limitation "therapeutic moiety", which is dependent on claim 9. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(1) Claims 9-10, 16-17, 20-24, 26-27, 30, 32-33 and 39 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,866,561 to Mark T. Ungs, issued February 2, 1999.

Ungs teaches a method for inducing angiogenesis in blood vessels proximal to stenosed regions, including application of an estrogen compound to the blood vessel walls at a treatment site proximal to or upstream of the stenosis (see abstract, in particular.) Ungs teaches that restenosis following PTCA is a signification problem, and that administration of estrogen to the stenosed, dilated region after PTCA has been suggested for the purposes of preventing restenosis (see column 1, lines 10-20 and 40-52, in particular), and thus teaches administration to an injured site, i.e. a vascular site that has been injured by PTCA. Ungs teaches that it is thus desirable to increase perfusion to heart tissue in place of or in addition to PTCA treatment (see column 1, lines 54-65, in particular.) Ungs teaches that a preferred method of treating stenosis involves application with a double walled drug delivery balloon catheter, as well as by coating a stent with an estrogen compound or by puncturing a vessel wall (see column 2, lines 5-45, in particular), and thus teaches administration with a device, as recited in claim 9. Ungs teaches that preferred estrogen compounds include 17-Beta estradiol (see column 4, lines 1-12, in particular), as in claim 9. Accordingly, Ungs teaches administration of 17-Beta estradiol in the lumen of a blood vessel having suffered vascular injury. There is no other therapeutic moiety disclosed that can be administered

other than the estrogen compound, preferably 17-Beta estradiol or estradoil (see column 4, lines 1, 10 and 11; claim 1).

Ungs does not specifically teach administration in the unit doses as recited in claims 9, 16-17, 24 and 26-27.

However, it is noted that Ungs teaches that 17Beta-estradiol is a preferred estrogen compound (see column 4, lines 1-11, in particular), and Ungs also teaches various methods of application of the estrogen via catheters, stents, etc, and refers to prior art catheter, for example, that are used for the local administration of drugs (see column 3, lines 1-15, in particular.) Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of 17Beta-estradiol provided in the method, according to the guidance provided by Ungs, to provide the desired treatment, such as the desired reduction in restenosis. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Accordingly, claims 9, 16-17, 24 and 26-27 are considered to be unpatentable over Ungs.

In regards to the limitation of reducing restenosis in claim 9, it is noted that as Ungs teaches administering the same compound via the same method as that instantly claimed, and to reduce the incidence of restenosis following a treatment such as PTCA that induces vascular injury, it is considered that the method of Ungs would necessarily also reduce restenosis in a patient having suffered vascular injury, as recited in the claim.

Regarding claims 10 and 30, Ungs teaches that the estrogen can be administered with an ionic carrier in an iontophoresis method using delivery balloon catheter (see column 2, lines 32-40, in particular.) Regarding claims 20-21 and 30, Ungs teaches administration of 17-Beta estradiol in the lumen of a blood vessel having suffered vascular injury, for example via catheter or a stent (see column 2, lines 5-45, in particular.)

Regarding claims 22-23 and 32-33, Ungs teaches that restenosis following PTCA is a significant problem (see column 1, lines 10-20, in particular), and teaches that treatment to increase perfusion to heart tissue, such as with estrogen compounds, are desirably performed in place of, or in addition to, PTCA (see column 1, lines 50-65, in particular.) Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the 17-beta estradiol following or simultaneously with the PTCA, based on the teachings of Ungs, with the expectation of increasing perfusion to heart tissue and for reducing the likelihood of restenosis.

(2) Claims 31 is rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,866,561 to Mark T. Ungs, issued February 2, 1999, as applied to claims 9-10, 16-17, 20-24, 26-27, 30 and 32-33 above, and further in view of U.S. Patent No. 5,439,446 to James Barry, issued August 8, 1995.

Ungs is applied as discussed above, and teaches the administration of 17beta-estradiol via device such as a stent or catheter for the treatment of restenosis.

Ungs does not specifically teach administering the 17beta-estradiol on a stent with a pharmaceutically acceptable carrier, as recited in claim 31.

Barry teaches a stent and therapeutic delivery system (see abstract, in particular.) Barry teaches that the stent can be used to provide active agents, and that the active agents can be provided by encapsulating in a dissolving material (pharmaceutically acceptable carrier), such as albumin or a polymer, to effect a continuing release from the stent. Thus, Barry teaches that it is known to provide a pharmaceutically acceptable carrier in combination with drug delivery from a stent.

Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the pharmaceutically acceptable carrier of Barry in the method of Ungs, because Ungs teaches delivering a

drug via a stent, and Barry teaches that it is known to provide pharmaceutically acceptable dissolving material with the delivery of drugs via a stent to provide continued release of the drug. Thus, one of ordinary skill in the art would have been motivated to provide the pharmaceutically acceptable dissolving carrier in the method of Ungs with the expectation of providing a desired release of the 17beta-estradiol drug.

Response to Arguments

Applicant's arguments with respect to the rejections of the claims have been fully considered.

> The Applicant argues the *Hirao* and *Kropa* cases cited in the pending Action do not support the position that reduction of restenosis is not entitled to patentable weight.

In light of the amendment to the claims, the Examiner agrees because the present claims are clear to read on a method of reducing restenosis.

> The Applicant argues that Ungs' solution to the problem is not to administer a 17-β estradiol in an amount effective to reduce restenosis to the site of dialation, but instead to avoid PTCA altogether. Therefore, Ungs teaches away from applicant's solution. Ungs states at column 1, lines 49-51 that "[a]dministration of estrogen to the stenosed, dilated region after PTCA has thus been suggested for the purposes of preventing restnosis," one would recognize that statement to be based not on any of Ungs' work, but simply a summary statement regarding the prior art disclosed in the Ungs patent. Thus, one of ordinary skill would be led away from the use of only a 17-β estradiol to reduce restenosis. Since the

use of a 17-β estradiol as claimed is not suggested by Ungs, the particular dose ranges discovered by the applicant are likewise inventive.

The Examiner disagrees because first, the statement, administration of estrogen to the stenosed, dilated region after PTCA has thus been suggested for the purposes of preventing restenosis, is a teaching as a whole of what is known in the art. Second, Ungs teaches administering the same compound via the same method as that instantly claimed, and to reduce the incidence of restenosis following a treatment such as PTCA that induces vascular injury, it is considered that the method of Ungs would necessarily also reduce restenosis in a patient having suffered vascular injury, as recited in the claim. Therefore, "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.) Accordingly, it is considered that one of ordinary skill in the art would have found it obvious to vary/and or optimize the amount of the estradiol provided, such as to achieve the amounts as claimed, with the expectation of providing a suitable restenosis treatment method.

The Applicant argues that the Stack Declaration of record reiterates that prevention of restenosis requires the inhibition of smooth muscle cell proliferation, as well as the promotion of vessel regeneration and repair. Further, that a compound may be known as capable of reducing proliferation of smooth muscle cells would not lead one to predict that such compound would also promote reendothelialization. Dr. Stack provides examples of compounds that inhibit proliferation, but no not promote reendothelization. The field is unpredictable, and the use of a 17-β estradiol as presently claimed would not have been suggested by Ungs. Ungs does not suggest the alleged inherent feature, and the Stack

> Declaration is further evidence that one would not have expected a 17-β estradiol to have the presently claimed effect. Moreover there is no evidence in Ungs that the presently claimed dose of estrogen was ever actually administered, likewise undercutting any inherency argument.

The Examiner disagrees because first, the current claims are drawn towards a method of reducing resenosis, not promoting reendothelialization. Second, since Ungs teaches administering the same compound via the same method steps as those instantly claimed, it is considered that the method of Ungs also necessarily improves reendothelization and vascular endothelial function. Third, the fact that applicant has recognized another advantage which would flow naturally from following the teachings or suggestion of the prior art cannot be the basis for patentability when the prior art teaches the invention or when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Fourth, actual proof that the estrogen compound was actually administered, such as through examples, is not required by the prior art.

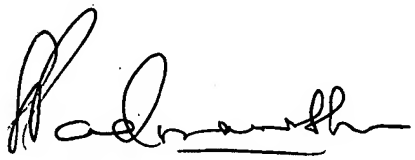
Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kendra D. Carter whose telephone number is (571) 272-9034. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KDC



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER